more clearly point out that which Applicants consider to be the claimed invention. Applicants have amended claim 1 to point out with even better clarity the specific process steps of the invention. Such amendments are considered remedial by the Examiner. Support for the proposed amendments is found in the specification as originally filed; hence, as the Examiner will appreciate, no new matter is being added by the proposed amendments. Therefore, entry of the amendments hereinabove and reconsideration of the Office Action mailed October 10, 2002 are respectfully requested.

4. Claims 1-35 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Specifically, the Examiner states that: "the invention appears to employ *Hansenula polymorpha* ATCC No. 74449. It is not clear if the written description is sufficiently repeatable to avoid the need for a deposit; and further, it is unclear if the starting materials were readily available to the public at the time of invention."

None of the microorganisms *per se* is claimed. *Hansenula polymorpha* ATCC No. 26012 is available from the ATCC, and was so at the time of filing of the Application (April 12, 2001) and at the time of filing of the application to which the Application claims priority (U.S. Provisional Patent Application No. 60/200,413 filed on April 12, 2000). Page 8, lines 8-12 of the present specification provide that *Hansenula polymorpha* ATCC No. 26012 was deposited by Pfizer Inc., the assignee of the present Application, on June 26, 1998, with the ATCC, under the terms of the Budapest Treaty, and given the deposit number of ATCC No. 74449. Page 8, lines 14-16 provide that all restrictions on the availability to the public of the microorganism culture so deposited will be irrevocably removed upon the issuance of a patent from the specification of the present invention, pursuant to 37 C.F.R. §1.808. Hence, all of the microorganisms are available to the public, or will be upon issuance of a patent from the present specification.

Applicant provides the following current ATCC catalog information in relation to *Hansenula polymorpha* ATCC No. 26012: Product Description (*Pichia angusta* (Teunisson et al.) Kurtzman, teleomorph deposited as *Hansenula polymorpha de Morais et Maia*, teleomorph Designation: DL-1 [*NRRL Y-7560*]), $140. Those skilled in the art will appreciate from the ATCC product description, that an additional source exists as well for obtaining *Hansenula polymorpha* ATCC No. 26012, i.e., NRRL Culture Collection Y-7560, Agricultural Research Service (ARS) (NRRL) Yeast Culture Collection, located at the National Center for Agricultural Utilization Research (NCAUR, Illinois) (the ARS Patent Culture Collection, specifically, the ARS Patent Culture Collection, is recognized as a depository under the Budapest Treaty). Hence, Applicants have fully complied with the requirements of 35 U.S.C. §112, first paragraph. Therefore, reconsideration of the Office Action mailed October 10, 2002 is respectfully requested.

5. Attached hereto is a marked-up version of the changes made to the claim by the current proposed amendments. The attached page is captioned "**Version with markings to show changes made**."

6. Applicants believe that the amendments hereinabove to claim 1 place the Application in condition for immediate allowance. Therefore, entry of the amendments hereinabove and reconsideration of the Office Action mailed October 10, 2002 are respectfully requested. Such prompt and favorable action is earnestly solicited.

Respectfully submitted,

Date: April 10, 2003

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CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service as First Class Mail in an envelope addressed to: Hon. Commissioner for Patents, Washington, D.C. 20231 on this 10th day of April, 2003.

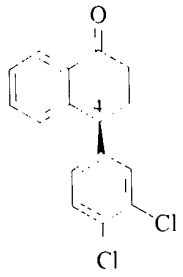
By: _____
Jennifer A. Kispert

## VERSION WITH MARKINGS TO SHOW CHANGES MADE

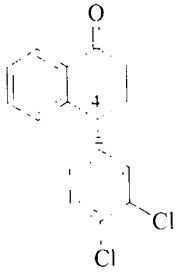
IN THE CLAIMS

Claim 1 is being amended as follows:

1. (Amended). A composition of matter prepared from a crude preparation of a microorganism, said microorganism selected from the group consisting of *Hansenula polymorpha* ATCC No. 26012, *Hansenula polymorpha* ATCC No. 74449, and such mutants thereof capable of accomplishing the stereoselective reduction of racemic 4-(3,4-dichlorophenyl)-3,4-dihydro-1(2H)-naphthalenone, where said racemic 4-(3,4-dichlorophenyl)-3,4-dihydro-1(2H)-naphthalenone is a mixture of (4S)-(3,4-dichlorophenyl)-3,4-dihydro-1(2H)-naphthalenone and (4R)-(3,4-dichlorophenyl)-3,4-dihydro-1(2H)-naphthalenone having the formulae

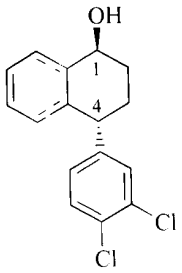



(4S)-(3,4-dichlorophenyl)-3,4-dihydro-1(2H)-naphthalenone, and

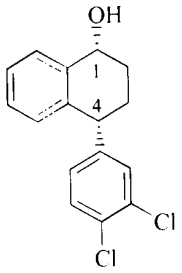



(4R)-(3,4-dichlorophenyl)-3,4-dihydro-1(2H)-naphthalenone,

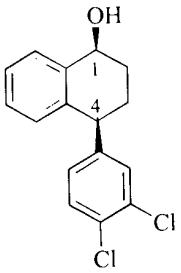
to a mixture of cis and trans tetralols having the formulae:



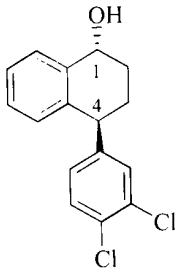

(trans) (1S, 4R) tetralol,




(cis) (1R, 4R) tetralol,




(cis) (1S, 4S) tetralol, and




(trans) (1R, 4S) tetralol,

where said reduction comprises: contacting said racemic 4-(3,4-dichlorophenyl)-3,4-dihydro-1(2H)-naphthalenone with said composition of matter; incubating the resulting mixture under conditions sufficient to yield said (trans) (1S, 4R) tetralol, said (cis) (1R, 4R) tetralol, said (trans) (1R, 4S) tetralol, and said (cis) (1S, 4S) tetralol, and to leave substantially unreacted said (4S)-(3,4-dichlorophenyl)-3,4-dihydro-1(2H)-naphthalenone; and recovering said unreacted (4S)-(3,4-dichlorophenyl)-3,4-dihydro-1(2H)-naphthalenone from said resulting mixture, by the process of: ~~comprising an enzyme activity and having the following identifying characteristics~~:

preparing a crude fraction of said microorganism by: contacting said microorganism with said racemic 4-(3,4-dichlorophenyl)-3,4-dihydro-1(2H)-naphthalenone under conditions sufficient to permit the induction of an enzyme activity capable of said reduction; centrifuging said microorganism; resuspending said centrifuged microorganism in a breaking buffer comprising beads; rupturing said microorganism in said breaking buffer under conditions sufficient to permit disruption of said microorganism and retention of said enzyme activity; centrifuging

said breaking buffer after said rupturing; retaining the supernatant of said centrifuged breaking buffer; and adding a protein stabilizing agent to said supernatant; ~~(a) present in a fraction from a crude preparation of *Hansenula polymorpha* ATCC No. 26012, *Hansenula polymorpha* ATCC No. 74449, or any other suitable mutant thereof, where said crude fraction is prepared by: inducing cells of *Hansenula polymorpha* ATCC No. 26012, *Hansenula polymorpha* ATCC *Hansenula polymorpha* ATCC No. 74449, or any other suitable mutant thereof, with an amount of the compound of Formula (I) under suitable conditions to permit the induction of the enzyme activity capable of stereoselectively reducing racemic tetralone to chiral tetralone, centrifuging said induced cells, resuspending said centrifuged cells in a breaking buffer comprising beads, rupturing said resuspended cells under suitable conditions to permit disruption of said cells and retention of an appreciable amount of said enzyme activity, centrifuging said breaking buffer after said rupturing, retaining the supernatant of said centrifuged breaking buffer, and adding a protein stabilizing agent to said supernatant;~~

recovering the proteins comprising said crude fraction by: adding a DNA precipitating agent to said crude fraction; centrifuging said crude extract containing said DNA precipitating agent; retaining the supernatant of said centrifuged crude extract; adding an amount of a protein precipitating agent to said supernatant of said centrifuged crude extract, where said amount of said protein precipitating agent permits about 48% fractional saturation; centrifuging said protein precipitating agent containing supernatant; retaining the supernatant of said centrifuged protein precipitating agent containing supernatant; adding an amount of a protein precipitating agent, where said amount of said protein precipitating agent permits about 75% fractional saturation; centrifuging said supernatant of said centrifuged protein precipitating agent containing supernatant; retaining the pellet resulting from said centrifugation; resuspending said pellet in a buffer; desalting said buffer; and concentrating the proteins comprising said resuspended pellet in said buffer; ~~(b) present in a fraction of the fraction described in (a) above, where said fraction is obtained by: adding a DNA precipitating agent to an amount of said fraction described~~

~~in (a) above, centrifuging said crude extract, retaining the supernatant of said centrifuged crude extract, adding a protein precipitating agent to said supernatant of said centrifuged crude extract to achieve about 48% fractional saturation, centrifuging said supernatant having about 48% fractional saturation, retaining said supernatant and adding a protein precipitating agent to said supernatant to achieve about 75% fractional saturation, centrifuging said supernatant having about 75% fractional saturation, retaining the pellet resulting from said centrifugation, resuspending the proteins comprising said pellet in a buffer and desalting and then concentrating said proteins in said buffer;~~

fractionating said resuspended proteins by: loading said resuspended proteins onto a column comprising a material having an affinity for dehydrogenases, where said material is capable of reversibly associating with said dehydrogenases; waiting for a sufficient period of time to permit the proteins of said resuspended proteins capable of associating with said material to associate with said material; eluting in fractions said proteins associated with said material using an NADPH gradient; assaying each of said eluted fractions for said enzyme activity by performing said reduction; and pooling said eluted fractions having said enzyme activity; ~~(c) present in a fraction of the fraction described in (b) above, where said fraction is obtained by: loading an amount of said fraction described in (b) above onto a column comprising a material capable of reversibly associating with said proteins comprising said fraction described in (b) and having said enzyme activity, eluting said reversibly associated proteins from said column using an NADPH gradient, assaying each eluted fraction for said enzyme activity, and pooling said eluted fractions having said enzyme activity;~~

fractionating said pooled eluted fractions by: desalting said pooled eluted fractions; loading said desalted pooled eluted fractions onto a column comprising an anion exchange material having an affinity for dehydrogenases, where said anion exchange material is capable of reversibly associating with said dehydrogenases; waiting for a sufficient period of time to permit the proteins of said desalted pooled eluted fractions capable of associating with said anion exchange material to associate

with said anion exchange material; eluting in fractions said proteins associated with said anion exchange material, where said eluting is by using a salt gradient; assaying each of said eluted fractions for said enzyme activity by performing said reduction; and pooling said eluted fractions having said enzyme activity; ~~(c) present in a fraction of the fraction described in (c) above, where said fraction is obtained by: desalting an amount of said fraction described in (c) above, loading an amount of said desalted fraction onto a column comprising an anion exchange material and capable of reversibly binding said proteins of said desalted fraction and having said enzyme activity, eluting said reversibly associated proteins from said column using a salt gradient, assaying each eluted fraction for said enzyme activity, and pooling said eluted fractions having said enzyme activity;~~

fractionating said pooled eluted fractions from said column comprising said anion exchange material by: desalting said pooled eluted fractions from said column comprising said anion exchange material; loading said pooled eluted fractions onto a column comprising a weak anion exchange material having an affinity for dehydrogenases, where said weak anion exchange material is capable of reversibly associating with said dehydrogenases; waiting for a sufficient period of time to permit the proteins of said desalted pooled eluted fractions capable of associating with said weak anion exchange material to associate with said weak anion exchange material; eluting in fractions said proteins associated with said weak anion exchange material, where said eluting is by using a salt gradient; assaying each of said eluted fractions for said enzyme activity by performing said reduction; and pooling said eluted fractions having said enzyme activity; ~~(e) present in a fraction of the fraction described in (d) above, where said fraction is obtained by: desalting an amount of said fraction described in (d) above, loading an amount of said fraction described in (d) above onto a column comprising a weak anion exchange material and capable of reversibly binding said proteins of said desalted fraction and having said enzyme activity, eluting said reversibly associated proteins from said column using a salt gradient, assaying each eluted fraction for said enzyme activity, and pooling said eluted fractions having said enzyme activity;~~

fractionating said pooled eluted fractions from said column comprising said weak anion exchange material by: desalting said pooled eluted fractions from said column comprising said weak anion exchange material; concentrating said desalted fractions; loading said concentrated fractions onto a column comprising a size exclusion material, where said size exclusion material is capable of allowing the separable elution of a fraction comprising a polypeptide having a molecular weight of from about 110,000 D to about 200,000 D; and eluting a fraction comprising a polypeptide having a molecular weight of from about 110,000 D to about 200,000 D; ~~and (f) present in a fraction of the fraction described in (e) above, where said fraction is obtained by: desalting an amount of said fraction described in (e) above, concentrating said desalted fraction, loading an amount of said concentrated fraction onto a column comprising a size exclusion material, and eluting a fraction comprising a polypeptide of from about 110,000 D to about 200,000 D and having said enzyme activity;~~ and

recovering said polypeptide from said fraction eluted from said column comprising said size exclusion material.

~~where said activity is present in said fractions when an amount of racemic tetralone is stereoselectively reduced to an amount of chiral tetralone.~~